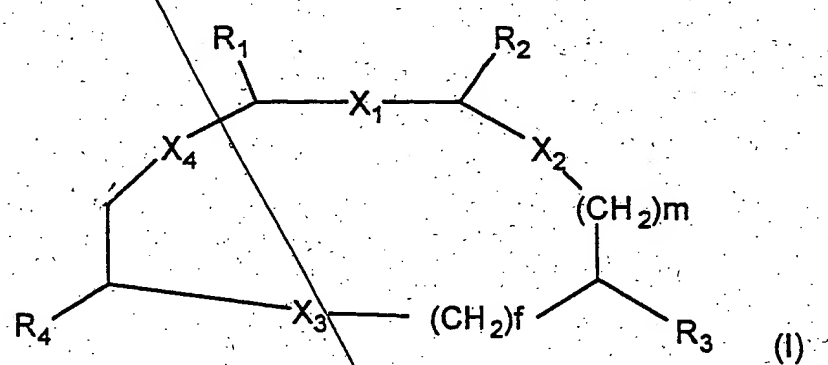
REMARKS

Please amend the application filed on even date herewith, prior to proceeding with its examination.

IN THE CLAIMS

Please cancel claims 1, 16, 17 and 18, without prejudice or disclaimer. Please add new claim 20, in lieu of claim 1, as follows:

--20. Monocyclic compounds of general formula (I)



(I)

wherein:

X_1, X_2, X_3, X_4, same or different, are a group chosen among: -CONR-, -NRCO-, $-CH_2$-NR-, -NR-CH_2- where R is H, C_{1-3} alkyl, benzyl;

f, m, same or different, are a number chosen among 0, 1 and 2;

R_1 and R_2, same or different, represent a group:

$-(CH_2)_r$-Ar where r = 0, 1, 2 and Ar is an aromatic group selected from the group consisting of benzene, naphthalene, thiophene, benzothiophene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole and benzoimidazole, optionally substituted with up to 2 substituents selected from the group consisting of C_{1-3} alkyl, halo C_{1-3} alkyl, C_{1-3} alkyloxy, C_{2-4} amino-alkyloxy, halogens, OH, NH_2, CN, and NR_6R_7, where R_6 and R_7 are the same or different and are H or C_{1-3} alkyl;

R_3 is selected from the group consisting of

$(CH_2)_r$-Ar_1 where r = 0, 1, 2 and Ar_1 is an aromatic compound selected from the group consisting of benzene, naphtalene, thiophene, benzothiophene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole and benzoimidazole,

optionally substituted with up to 2 substitutents selected from the group consisting of C_{1-3} alkyl, halo C_{1-3} alkyl, C_{1-3} alkyloxy, amino-alkyloxy, halogens, OH, NH_2, and NR_6R_7, where R_6 and R_7 are the same or different, and are H or C_{1-3} alkyl,

R_4 is a member selected from the group consisting of:

- NR_8R_9, where R_8 is H or C_{1-3} alkyl; and

R_9 is a methanesulfonyl, tosyl, tetrahydropyranyl, tetrahydrothiopyranyl, optionally mono or di-substituted by oxygen on the S atom, piperidyl optionally substituted on the N-atom by a C_{1-3} alkyl, C_{1-3} acyl, aminosulfonyl, methanesulfonyl; or a group (CH2)g-R_{10}, where g is 1, 2, 3 and R_{10} is selected from the group consisting of morpholine, furan, CN;

or R_8 and R_9 together with the N atom to which they are linked form a piperazine, optionally substituted on one of its nitrogens by a C_{1-3} alkyl, C_{1-3} acyl or methanesulfonyl;

$-N(R_{11})CO(CH_2)_h-R_{12}$ where R_{11} is H, C_{1-3} alkyl; h is 0,1,2,3; and R_{12} is selected from the group consisting of morpholine, pyrrolidine optionally substituted with an hydroxy or hydroxymethyl, piperidine optionally substituted with a hydroxy carboxyamido or aminosulfonyl group, piperazine optionally substituted on the N-atom by C_{1-3} alkyl, triazole, tetrazole, 5-mercapto-tetrazole, furan, thiophene, thiomorpholine optionally mono or di-oxygenated on the S-atom, amino-cyclohexane optionally substituted by an hydroxy group;

- COR_{13} wherein R_{13} is a member selected from the group consisting of morpholine and piperazine, optionally substituted by a C_{2-6} alkyl containing one or more ether or hydroxy groups;

as enantiomers or mixture of diastereoisomers, and their pharmaceutically acceptable salts.

Please amend the following claims:

2. (Amended) Compound according to claim [1] 20 wherein:

f is 1

m is 0

X_1, X_2, X_3, X_4, are the same or different and are [a group] a member selected from the group consisting of -CONR- and NRCO-,

where R is H or methyl,

R_1 and R_2 are the same or different, are:

$-CH_2$-Ar wherein Ar is an aromatic group [chosen among] selected from the group consisting of benzene, pyridine, indole, [possibly] optionally substituted with up to two residues, with substituents [chosen among] selected from the group consisting of:

C_{1-3} alkyl [and], halo C_{1-3} alkyl, C_{1-3} alkyloxy, C_{2-4} amino alkyloxy, halogens, OH, NH_2, CN, NR_6R_7, where R_6 and R_7, are the same or different, and are H or C_{1-3} alkyl;

R_3 is $-CH_2-Ar_1$, wherein Ar_1 is an aromatic group selected from the group consisting of: [alfa] alpha naphthyl, beta naphthyl, phenyl, phenyl substituted with up to two residues [chosen among] selected from the group consisting of C_{1-3} alkyl, [and] halo C_{1-3} alkyl, C_{1-3} alkyloxy, halogens, OH, NH_2[,].

[R_4 is as defined in Claim 1]

3. (Amended) Compounds according to claim 2 wherein:

$-X_1$, X_2, X_3, X_4 are -CON[R]H-,

[R is H]

A2 Cont

$-R_1$ is the lateral chain of tryptophan;

$-R_2$ is the lateral chain of phenylalanine [possibly] optionally substituted with up to two residues [chosen among] selected from the group consisting of: chlorine, fluorine, CF_3, OH, CN[; or a group] 3-pyridyl-methyl[; or a group] and 4-pyridyl-methyl;

$-R_3$ is benzyl.

[and f, m and R_4 are as defined in claim 2]

4. (Amended) Compounds according to claim 3 wherein:

[R, R1, R2, R3, f, m are as above defined and:]

R_4 is a group NR_8R_9 wherein:

R_8 is H or methyl;

R_9 is [a group chosen among:] [:] selected from the group consisting of 4-tetrahydropyranyl, 4-tetrahydrothiopyranyl, 1-oxo-tetrahydrothiopyran-4-yl, 1,1-dioxo-tetrahydrothiopyran-4-yl, N-methyl-4-piperidinyl, N-metansulfonyl-4-piperidinyl, N-aminosulfonyl-4-piperidinyl,

A2 cont

or R_8 and R_9 together with the N atom to which they are linked represent: N-methyl-piperaziniyl, N-acetyl-piperazinyl, piperazinyl, N-methanesulfonyl-piperazinyl

6. (Amended) Compound according to Claim 3 wherein:

R_4 represents a group NR_8R_9, where R_8 is H and R_9 is chosen among: methanesulfonyl, tosyl,

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a group $(CH_2)g\text{-}R_{10}$ wherein g is 1, 2 and R_{10} is chosen among: morpholine, furan, CN.

[and f, m, X_1, X_2, X_3, X_4, R, R_1, R_2 and R_3 are as defined in claim 3]

8. (Amended) Compounds according to claim 3 wherein:

[R4] $\underline{R_4}$ is a group - $N(R_{11})CO(CH_2)_h\text{-}R_{12}$ wherein R_{11} is H, h is 0 or 1, and [R12] $\underline{R_{12}}$ is [chosen among.:] <u>selected from the group consisting of</u> 1-tetrazolyl, 5-mercapto-tetrazol-1-yl, 1-

A4

triazolyl, furanyl, thiophenyl, morpholine, 4-hydroxy-piperidine, 4-carboxyamido-piperidine, 3-hydroxy-pyrrolidine, 2-hydroxymethylpyrrolidine, 4-methyl-piperazine, 4-aminosulfonyl-piperazine, 1-oxo-thiomorpholine, 4-hydroxy-cyclohexan-1-yl-amino.

[and f, m, X_1, X_2, X_3, X_4, R, R_1, R_2 and R_3 are as defined in claim 3]

10. (Amended) Compounds according to Claim 3 wherein:

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[R4] $\underline{R_4}$ represents a group COR_{13} wherein R_{13} is a [group chosen among] <u>member selected from the group consisting of</u> morpholine and 4-(hydroxyethyloxyethyl)-piperazine.

[and f, m, X_1, X_2, X_3, X_4, R, R_1, R_2 and R_3 are as defined in claim 3]

12. (Amended) Pharmaceutical compositions containing as active principle

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compounds of general formula (1) according to Claim [1] <u>20</u> in combination with pharmaceutically acceptable carriers or excipients.

IN THE SPECIFICATION

Page 4, line 6, after "alkyl" first occurrence, insert --,--; line 6, delete "and"; delete "haloalkyl" and insert --halo C_{1-3} alkyl--.

Page 4, line 10, after "alkyl", insert --,--;

Page 4, line 11, delete "and";

Page 4, line 11, delete "haloalkyl"; insert --halo C_{1-3} alkyl--.

Page 5, line 3, delete "-CONR-", insert -- -CONH- --.

Page 5, line 3, delete "-R is H;"

Please cancel original pages 1 and 1a, copies enclosed, and substitute enclosed new pages 1 and 1a.

REMARKS

It is respectfully requested that the examination proceed on the basis of the amendatory action taken herein and that this amendment be entered prior to calculating the filing fee and according the application a filing date.

Respectfully submitted,

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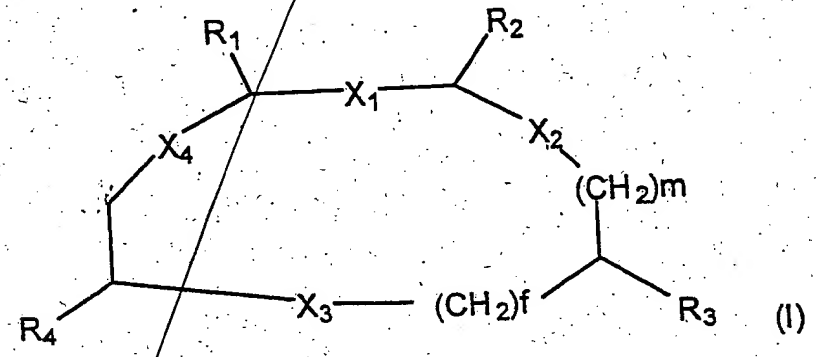
MONOCYCLIC COMPOUNDS HAVING NK-2 ANTAGONIST ACTION AND COMPOSITIONS CONTAINING THEM

FIELD OF THE INVENTION

The present invention refers to compound of general formula (I)



(I)

wherein:

X_1, X_2, X_3, X_4, same or different, are a group chosen among: -CONR-, -NRCO-, $-CH_2-NR-$, $-NR-CH_2-$ where R is H, C_{1-3} alkyl, benzyl;

f, m, same or different, are a number chosen among 0,1 and 2;

R_1 and R_2, same or different, are a group:

$-(CH_2)_r-Ar$ where r = 0, 1, 2 and Ar is an aromatic group chosen among: benzene, naphthalene, thiophene, benzothiophene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole, benzoimidazole, possibly substituted with up to 2 substituents chosen

among C_{1-3} alkyl, halo C_{1-3} alkyl, C_{1-3} alkyloxy, amino-alkyloxy, halogens, OH, NH_2, NR_6R_7, where R_6 and R_7, are the same or different, and are H or C_{1-3} alkyl,

R_3 is a member selected from the group consisting of:

- $(CH_2)_r$-Ar_1 where r = 0, 1, 2 and Ar_1 is an aromatic group selected from the group consisting of: benzene, naphtalene, thiophene, benzothiophene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole, benzoimidazole, possibly substituted with up to 2 groups selected from the group consisting of C_{1-3} alkyl, halo C_{1-3} alkyl, C_{1-3} alkyloxy and amino-alkyloxy, halogens, OH, NH_2, NR_6R_7, where R_6 and R_7, are the same or different, and are H or C_{1-3} alkyl,

R_4 is a group chosen among: